Antibodies

A LABORATORY MANUAL

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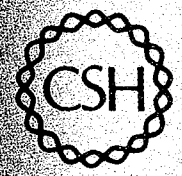

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The interaction of an antibody with an antigen forms the basis of all immunochemical techniques. This chapter discusses the properties of the antibody–antigen interaction and is divided into three sections. The first summarizes the structure of the antibody–antigen bonds, the second covers the strength of these interactions, a characteristic known as affinity, and the third presents the factors that contribute to the overall stability of immune complexes, a property called avidity.

STRUCTURE OF THE ANTIBODY–ANTIGEN COMPLEX

The structure of the antibody–antigen complex has been studied by measuring the affinity of binding between an antibody and a series of related antigens, by using affinity labeling reagents, by site-directed mutagenesis of the antibody combining site, by molecular modeling, and, most compellingly, by X-ray diffraction studies of antibody–antigen cocrystals. Together, these techniques have delineated the region of the antibody molecule that is involved in antigen binding, the region of the antigen molecule that interacts with the antibody, and the molecular basis for antibody specificity.

The antigen binding site of an antibody is formed by the variable regions of the heavy and light chains

Affinity labeling and X-ray crystallography of immune complexes have established that the antigen binding site is formed by the heavy- and light-chain variable regions (see Fig. 2.5). The two variable regions are closely associated and are bound to each other by noncovalent interactions. The remainder of the heavy and light chains forms other domains that are not involved in antigen binding (see Chapter 2). The amino acids forming the antigen binding site are derived from both the heavy and light chains and correspond to the amino acids of the hypervariable regions determined from protein sequencing. The hypervariable regions are known as the complementarity determining regions (CDRs). There are six CDRs, three on each chain, and they form discrete loops anchored and oriented by the framework residues of the variable domains (Fig. 3.1).

The region of an antigen that binds to an antibody is called an epitope

The region of an antigen that interacts with an antibody is defined as an epitope. An epitope is not an intrinsic property of any particular